

### REMARKS

Claims 31, 36-38, 40-51, 54-55, as amended, are pending in this application for the Examiner's review and consideration. Claims 32-35, 39, 52-53, 56-57 were canceled without prejudice. Applicants reserve the right to file one or more divisional or continuation applications directed to the subject matter of the canceled claims or other unclaimed subject matter. Claim 31, 42, 43, 47, 48, 49, and 54 were amended to limit the scope of the claim to Ar representing pyridyl. Claim 54 was written in independent form. No new matter has been introduced by these claim amendments so that their entry at this time is warranted.

The Examiner required restriction between Group I, claims 31-34, 36-38, 40-47, and 54-55, wherein Ar is pyridyl, drawn to pyridines, classified in class 514, 546, subclasses various; Group II, claims 35, 39, 31-32, 36-47, and 54-55, wherein Ar is a carbocyclic ring, drawn to coumarins, classified in class 514, 549, subclasses various; Group III, claims 31-34, 36-38, 40-47, 54-55 of the remaining compounds, drawn to various organic compounds, classified in class 514, 546, 544, 548, subclasses various; Group IV, claims 48-51, drawn to a method of using a different scope from the compounds classified in class 514, subclasses various; Group V, claims 52-53 drawn to a method of using with additional antineoplastic agents, classified in class 514, subclasses various; and Group VI, claims 56-57, drawn to a composition with one or more antineoplastic agents, classified in class 514, subclasses various.

Applicants provisionally elect, with traverse, the claims of Group I, claims 31-34, 36-38, 40-47, and 54-55, wherein Ar is pyridyl. Applicants respectfully submit that, at the least, claims 48-51 and 54-55 should also be included in the claims of Group I. Claims 48-51 and 54-55 should be Examined with the claims of Group I since these claims are simply method claims (claims 48-51 and 54) or pharmaceutical composition claims (claim 55) using the composition of claim 31, with the exception that the method claims do not include the proviso recited in claim 31.

No fee is believed to be due for the submission of this response. Should any fees be required, please charge such fees to Pennie & Edmonds deposit account no. 16-1150.

Respectfully submitted,

Date May 22, 2003



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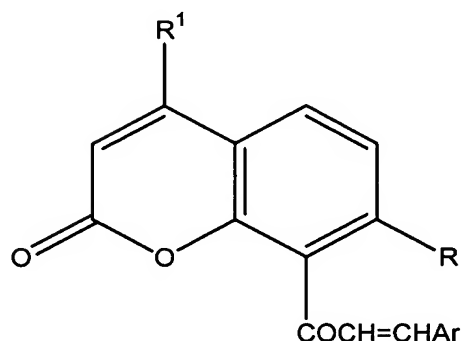
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## Appendix A

### Changes to the Claims

Application No.: 10/075,625; Filed: February 15, 2002

31. (currently amended) A compound of Formula (I):



(I)

or a pharmaceutically acceptable salt or solvate thereof wherein:

Ar represents: pyridyl which ~~a substituted or unsubstituted, aromatic or non-aromatic, carbocyclic or heterocyclic group having from 5 to 10 ring atoms or two rings with each ring containing 5 or 6 ring atoms, wherein the heterocyclic group comprises a heteroatom selected from N, O and S, and wherein the carbocyclic or heterocyclic group may be unsubstituted or substituted with one or more substituents selected from the group consisting of: (a) Cl, (b) Br, (c) F, (d) OH, (e) NO<sub>2</sub>, (f) CF<sub>3</sub>, (g) C<sub>1-4</sub> alkyl, (h) SCH<sub>3</sub>, (i) NHCOCH<sub>3</sub>, (j) N(R<sup>6</sup>)(R<sup>8</sup>) wherein R<sup>6</sup> and R<sup>8</sup> are the same or different and each represents H or C<sub>1-4</sub> alkyl, (k) OR<sup>10</sup> wherein R<sup>10</sup> represents a saturated or unsaturated C<sub>1-6</sub> straight or branched hydrocarbonyl group which may be unsubstituted or substituted with from 1 to 3 substituents selected from Cl, Br, F, OMe, NO<sub>2</sub> and CF<sub>3</sub>, and (l) -OCOR<sup>11</sup> wherein R<sup>11</sup> represents a saturated or unsaturated C<sub>1-6</sub> straight or branched hydrocarbonyl group or a phenyl group;~~

R represents OH, OR<sup>10</sup> or OCOR<sup>11</sup> wherein R<sup>10</sup> and R<sup>11</sup> are as defined above; and R<sup>1</sup> represents H or a C<sub>1-6</sub> straight or branched hydrocarbonyl group which may be unsubstituted or substituted with from 1 to 3 substituents selected from Cl, Br, F, OMe, NO<sub>2</sub> and CF<sub>3</sub>

with the proviso that when R<sup>1</sup> is CH<sub>3</sub> and R is OH, then Ar cannot be 4-pyridyl, ~~4-methylphenyl, 3-nitrophenyl, 3-methoxy-4-ethoxyphenyl, 3-methoxy-4-n-butoxyphenyl, 4-(N,N-dimethylamino)phenyl, 2-hydroxy-3,5-dibromophenyl, 2-hydroxy-5-methylphenyl, 4-chlorophenyl, phenyl, 3-methoxyphenyl, 4-methoxyphenyl, or 4-dimethoxyphenyl;~~

~~—— (ii) when R<sup>1</sup> is CH<sub>3</sub> and R is OCOCH<sub>3</sub>, the group, then Ar cannot be 4-methoxyphenyl, 3,4 dimethoxyphenyl, 4 (N,N dimethylamino)phenyl, 3-methoxy 4-acetoxyphenyl, 3,4,5 trimethoxyphenyl, or 2-chlorophenyl;~~  
~~—— (iii) when R<sup>1</sup> is phenyl or H and R is OCH<sub>3</sub> or OH, then Ar cannot be 4-methoxyphenyl; and~~  
~~—— (iv) when R<sup>1</sup> is CH<sub>3</sub> and R is OCH<sub>3</sub> or OH, then Ar cannot be 4-methoxyphenyl or 3,4 dimethoxyphenyl.~~

42. (currently amended) The compound of claim 31, wherein Ar is selected from phenyl, trimethoxyphenyl, 3-pyridyl, and 4-pyridyl, and 3-indyl; and R is selected from OCH=C(CH<sub>3</sub>)<sub>2</sub>, OCH<sub>2</sub>CMe=CH<sub>2</sub>, OCH<sub>2</sub>CH=CH<sub>2</sub> or OCH<sub>2</sub>C≡CH.

43. (currently amended) The compound of claim 31 ~~35~~, wherein Ar is selected from phenyl, which may be unsubstituted or substituted with from 1 to 3 substituents independently selected from Cl, Br, F, OMe, NO<sub>2</sub>, CF<sub>3</sub>, C<sub>1-4</sub> alkyl, NMe<sub>2</sub>, NEt<sub>2</sub>, SCH<sub>3</sub>, and NHCOCH<sub>3</sub>; thienyl; 2-furyl; 3-pyridyl; and 4-pyridyl; or indyl; and

R is selected from OH or OCH<sub>2</sub>R<sup>1</sup>, wherein R<sub>1</sub> is selected from -CH=CMe<sub>2</sub>, -CMe=CH<sub>2</sub>, -CH=CH<sub>2</sub> and -C≡CH.

47. (currently amended) The compound of claim 31, selected from the group consisting of:

1-[4-methyl-7-(3-methylbut-2-enyloxy)coumarin-8-yl]-3-(pyridine-3-yl)propen-1-one;  
~~1-[4-methyl-7-(3-methylbut-2-enyloxy)coumarin-8-yl]-3-phenylpropen-1-one;~~  
~~1-[4-methyl-7-(3-methylbut-2-enyloxy)coumarin-8-yl]-3-(3,4,5-trimethoxyphenyl)-propen-1-one;~~  
 1-[4-methyl-7-(2-methylallyloxy)coumarin-8-yl]-3-(pyridine-3-yl)propen-1-one;  
~~1-[4-methyl-7-(2-methylallyloxy)coumarin-8-yl]-3-phenylpropen-1-one;~~  
~~1-[4-methyl-7-(2-methylallyloxy)coumarin-8-yl]-3-(3-methoxyphenyl)propen-1-one;~~  
~~1-[4-methyl-7-(2-methylallyloxy)coumarin-8-yl]-3-(3,4,5-trimethoxyphenyl)propen-1-one;~~  
~~1-[4-methyl-7-(allyloxy)coumarin-8-yl]-3-phenylpropen-1-one;~~  
 1-[4-methyl-7-(allyloxy)coumarin-8-yl]-3-(pyridine-3-yl)propen-1-one; and  
~~1-[4-methyl-7-(allyloxy)coumarin-8-yl]-3-(3-methoxyphenyl)propen-1-one;~~

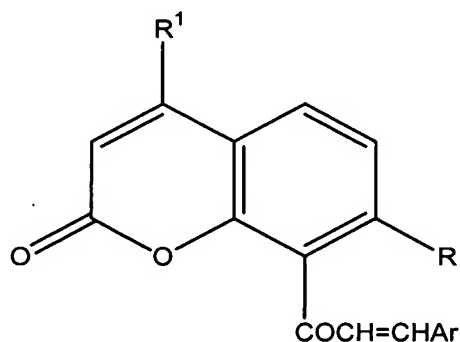
~~1-[4-methyl-7-(allyloxy)coumarin-3-yl]-3-(3,4,5-trimethoxyphenyl)propen-1-one;~~  
~~1-[4-methyl-7-(prop-2-ynyloxy)coumarin-8-yl]-3-(3,4,5-trimethoxyphenyl)propen-~~  
~~1-one;~~

~~1-[4-methyl-7-(prop-2-ynyloxy)coumarin-8-yl]-3-phenylpropen-1-one;~~

~~1-[4-methyl-7-(prop-2-ynyloxy)coumarin-8-yl]-3-(pyridin-3-yl)propen-1-one; and~~

~~1-[4-methyl-7-(prop-2-ynyloxy)coumarin-8-yl]-3-(3-methoxyphenyl)propen-1-one.~~

48. (currently amended) A method of treating cancer in a patient comprising administering to the patient a compound of formula:



or a pharmaceutically acceptable salt or solvate thereof wherein:

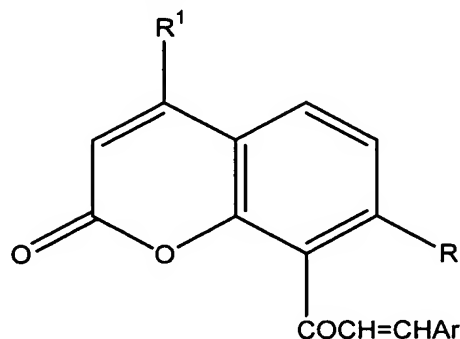
Ar represents: pyridyl ~~which a substituted or unsubstituted, aromatic or non-aromatic, carbocyclic or heterocyclic group having from 5 to 10 ring atoms or two rings with each ring containing 5 or 6 ring atoms, wherein the heterocyclic group comprises a heteroatom selected from N, O and S, and wherein the carbocyclic or heterocyclic group may be unsubstituted or substituted with one or more substituents selected from the group consisting of: (a) Cl, (b) Br, (c) F, (d) OH, (e) NO<sub>2</sub>, (f) CF<sub>3</sub>, (g) C<sub>1-4</sub> alkyl, (h) SCH<sub>3</sub>, (i) NHCOCH<sub>3</sub>, (j) N(R<sup>6</sup>)(R<sup>8</sup>) wherein R<sup>6</sup> and R<sup>8</sup> are the same or different and each represents H or C<sub>1-4</sub> alkyl, (k) OR<sup>10</sup> wherein R<sup>10</sup> represents a saturated or unsaturated C<sub>1-6</sub> straight or branched hydrocarbyl group which may be unsubstituted or substituted with from 1 to 3 substituents selected from Cl, Br, F, OMe, NO<sub>2</sub> and CF<sub>3</sub>, and (l) -OCOR<sup>11</sup> wherein R<sup>11</sup> represents a saturated or unsaturated C<sub>1-6</sub> straight or branched hydrocarbyl group or a phenyl group;~~

R represents OH, OR<sup>10</sup> or OCOR<sup>11</sup> wherein R<sup>10</sup> and R<sup>11</sup> are as defined above; and

R¹ represents H or a C<sub>1-6</sub> straight or branched hydrocarbyl group which may be unsubstituted or substituted with from 1 to 3 substituents selected from Cl, Br, F, OMe, NO<sub>2</sub> and CF<sub>3</sub>.

no proviso

49. (currently amended) A method of treating or preventing neoplasms in a patient comprising administering to the patient a compound of formula:



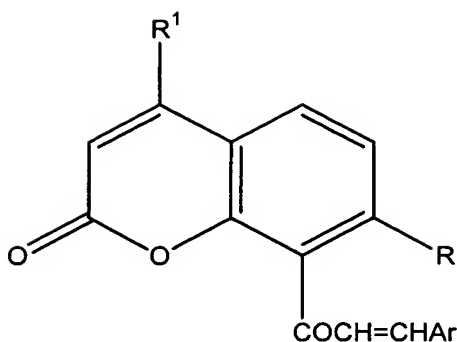
or a pharmaceutically acceptable salt or solvate thereof wherein:

Ar represents: ~~pyridyl a substituted or unsubstituted, aromatic or non aromatic, carbocyclic or heterocyclic group having from 5 to 10 ring atoms or two rings with each ring containing 5 or 6 ring atoms, wherein the heterocyclic group comprises a heteroatom selected from N, O and S, and wherein the carbocyclic or heterocyclic group may be unsubstituted or~~ substituted with one or more substituents selected from the group consisting of: (a) Cl, (b) Br, (c) F, (d) OH, (e) NO<sub>2</sub>, (f) CF<sub>3</sub>, (g) C<sub>1-4</sub> alkyl, (h) SCH<sub>3</sub>, (i) NHCOCH<sub>3</sub>, (j) N(R<sup>6</sup>)(R<sup>8</sup>) wherein R<sup>6</sup> and R<sup>8</sup> are the same or different and each represents H or C<sub>1-4</sub> alkyl, (k) OR<sup>10</sup> wherein R<sup>10</sup> represents a saturated or unsaturated C<sub>1-6</sub> straight or branched hydrocarbyl group which may be unsubstituted or substituted with from 1 to 3 substituents selected from Cl, Br, F, OMe, NO<sub>2</sub> and CF<sub>3</sub>, and (l) -OCOR<sup>11</sup> wherein R<sup>11</sup> represents a saturated or unsaturated C<sub>1-6</sub> straight or branched hydrocarbyl group or a phenyl group;

R represents OH, OR<sup>10</sup> or OCOR<sup>11</sup> wherein R<sup>10</sup> and R<sup>11</sup> are as defined above; and

R<sup>1</sup> represents H or a C<sub>1-6</sub> straight or branched hydrocarbyl group which may be unsubstituted or substituted with from 1 to 3 substituents selected from Cl, Br, F, OMe, NO<sub>2</sub> and CF<sub>3</sub>.

54. (currently amended) A method of treating or preventing menopausal disorders and osteoporosis in a patient comprising administering to the patient a compound of ~~claim 31~~ formula:



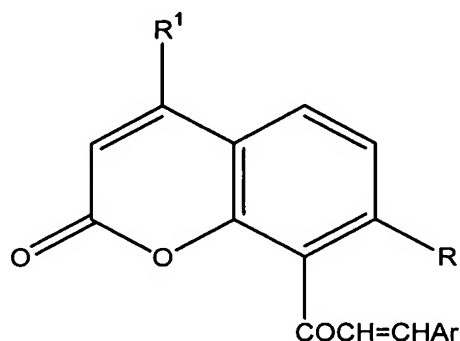
or a pharmaceutically acceptable salt or solvate thereof wherein:

Ar represents: pyridyl which may be unsubstituted or substituted with one or more substituents selected from the group consisting of: (a) Cl, (b) Br, (c) F, (d) OH, (e) NO<sub>2</sub>, (f) CF<sub>3</sub>, (g) C<sub>1-4</sub> alkyl, (h) SCH<sub>3</sub>, (i) NHCOCH<sub>3</sub>, (j) N(R<sup>6</sup>)(R<sup>8</sup>) wherein R<sup>6</sup> and R<sup>8</sup> are the same or different and each represents H or C<sub>1-4</sub> alkyl, (k) OR<sup>10</sup> wherein R<sup>10</sup> represents a saturated or unsaturated C<sub>1-6</sub> straight or branched hydrocarbyl group which may be unsubstituted or substituted with from 1 to 3 substituents selected from Cl, Br, F, OMe, NO<sub>2</sub> and CF<sub>3</sub>, and (l) -OCOR<sup>11</sup> wherein R<sup>11</sup> represents a saturated or unsaturated C<sub>1-6</sub> straight or branched hydrocarbyl group or a phenyl group;

R represents OH, OR<sup>10</sup> or OCOR<sup>11</sup> wherein R<sup>10</sup> and R<sup>11</sup> are as defined above; and R<sup>1</sup> represents H or a C<sub>1-6</sub> straight or branched hydrocarbyl group which may be unsubstituted or substituted with from 1 to 3 substituents selected from Cl, Br, F, OMe, NO<sub>2</sub> and CF<sub>3</sub>.

**Appendix B**  
Currently Pending Claims  
Application No.: 10/075,625; Filed: February 15, 2002

31. (currently amended)      A compound of Formula (I):



or a pharmaceutically acceptable salt or solvate thereof wherein:

Ar represents: pyridyl which may be unsubstituted or substituted with one or more substituents selected from the group consisting of: (a) Cl, (b) Br, (c) F, (d) OH, (e) NO<sub>2</sub>, (f) CF<sub>3</sub>, (g) C<sub>1-4</sub> alkyl, (h) SCH<sub>3</sub>, (i) NHCOCH<sub>3</sub>, (j) N(R<sup>6</sup>)(R<sup>8</sup>) wherein R<sup>6</sup> and R<sup>8</sup> are the same or different and each represents H or C<sub>1-4</sub> alkyl, (k) OR<sup>10</sup> wherein R<sup>10</sup> represents a saturated or unsaturated C<sub>1-6</sub> straight or branched hydrocarbyl group which may be unsubstituted or substituted with from 1 to 3 substituents selected from Cl, Br, F, OMe, NO<sub>2</sub> and CF<sub>3</sub>, and (l) -OCOR<sup>11</sup> wherein R<sup>11</sup> represents a saturated or unsaturated C<sub>1-6</sub> straight or branched hydrocarbyl group or a phenyl group;

R represents OH, OR<sup>10</sup> or OCOR<sup>11</sup> wherein R<sup>10</sup> and R<sup>11</sup> are as defined above; and R<sup>1</sup> represents H or a C<sub>1-6</sub> straight or branched hydrocarbyl group which may be unsubstituted or substituted with from 1 to 3 substituents selected from Cl, Br, F, OMe, NO<sub>2</sub> and CF<sub>3</sub>.

32. (canceled)

33. (canceled)

34. (canceled)

35. (canceled)

36. (original) The compound of claim 31, wherein the substituents on the Ar group are selected from the group consisting of: NHCOCH<sub>3</sub>, N(R<sup>8</sup>)(R<sup>8</sup>), OR<sup>10</sup>, and -OCOR<sup>11</sup>.

37. (original) The compound of claim 31, wherein Ar is substituted with one or more OR<sup>10</sup> groups and R<sup>10</sup> is a saturated or unsaturated C<sub>1-6</sub> straight or branched hydrocarbyl group.

38. (original) The compound of claim 37, wherein R<sup>10</sup> is methyl.

39. (canceled)

40. (original) The compound of claim 31, wherein R is an unsaturated C<sub>1-6</sub> straight or branched hydrocarbyl group.

41. (original) The compound of claim 40, wherein R is OCH=C(CH<sub>3</sub>)<sub>2</sub>, OCH<sub>2</sub>CMe=CH<sub>2</sub>, OCH<sub>2</sub>CH=CH<sub>2</sub>, or OCH<sub>2</sub>C≡CH.

42. (currently amended) The compound of claim 31, wherein Ar is selected from 3-pyridyl, and 4-pyridyl; and R is selected from OCH=C(CH<sub>3</sub>)<sub>2</sub>, OCH<sub>2</sub>CMe=CH<sub>2</sub>, OCH<sub>2</sub>CH=CH<sub>2</sub> or OCH<sub>2</sub>C≡CH.

43. (currently amended) The compound of claim 31, wherein Ar is selected from 3-pyridyl and 4-pyridyl and R is selected from OH or OCH<sub>2</sub>R<sup>1</sup>, wherein R<sub>1</sub> is selected from -CH=CMe<sub>2</sub>, -CMe=CH<sub>2</sub>, -CH=CH<sub>2</sub> and -C≡CH.

44. (original) The compound of claim 31, wherein R<sup>6</sup> and R<sup>8</sup> are the same or different and each is independently H or C<sub>1-4</sub> alkyl.

45. (original) The compound of claim 31, wherein R<sup>10</sup> and R<sup>11</sup> are each independently a saturated or unsaturated C<sub>1-6</sub> straight chain or branched hydrocarbyl group.

46. (original) The compound of claim 45, wherein R<sup>10</sup> and R<sup>11</sup> are selected from methyl, ethyl, n-propyl, and isopropyl.

47. (currently amended) The compound of claim 31, selected from the group consisting of:

1-[4-methyl-7-(3-methylbut-2-enyloxy)coumarin-8-yl]-3-(pyridine-3-yl)propen-1-one;

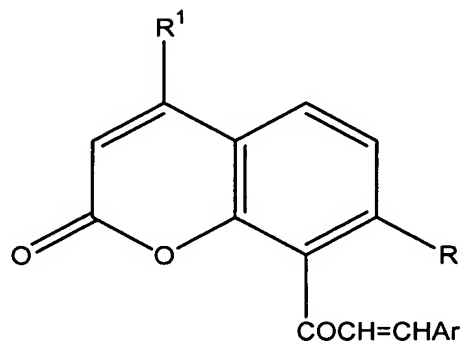
1-[4-methyl-7-(2-methylallyloxy)coumarin-8-yl]-3-(pyridine-3-yl)propen-1-one;

1-[4-methyl-7-(allyloxy)coumarin-8-yl]-3-(pyridine-3-yl)propen-1-one; and

1-[4-methyl-7-(prop-2-ynyloxy)coumarin-8-yl]-3-(pyridine-3-yl)propen-1-one.



48. (currently amended) A method of treating cancer in a patient comprising administering to the patient a compound of formula:

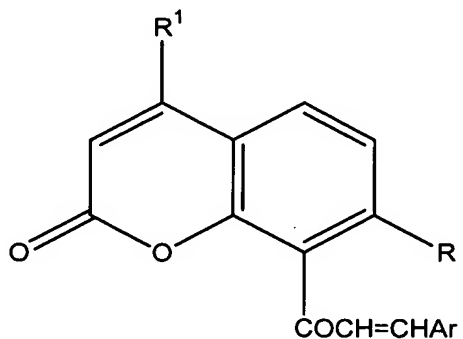


or a pharmaceutically acceptable salt or solvate thereof wherein:

Ar represents: pyridyl may be unsubstituted or substituted with one or more substituents selected from the group consisting of: (a) Cl, (b) Br, (c) F, (d) OH, (e) NO<sub>2</sub>, (f) CF<sub>3</sub>, (g) C<sub>1-4</sub> alkyl, (h) SCH<sub>3</sub>, (i) NHCOCH<sub>3</sub>, (j) N(R<sup>6</sup>)(R<sup>8</sup>) wherein R<sup>6</sup> and R<sup>8</sup> are the same or different and each represents H or C<sub>1-4</sub> alkyl, (k) OR<sup>10</sup> wherein R<sup>10</sup> represents a saturated or unsaturated C<sub>1-6</sub> straight or branched hydrocarbyl group which may be unsubstituted or substituted with from 1 to 3 substituents selected from Cl, Br, F, OMe, NO<sub>2</sub> and CF<sub>3</sub>, and (l) -OCOR<sup>11</sup> wherein R<sup>11</sup> represents a saturated or unsaturated C<sub>1-6</sub> straight or branched hydrocarbyl group or a phenyl group;

R represents OH, OR<sup>10</sup> or OCOR<sup>11</sup> wherein R<sup>10</sup> and R<sup>11</sup> are as defined above; and R<sup>1</sup> represents H or a C<sub>1-6</sub> straight or branched hydrocarbyl group which may be unsubstituted or substituted with from 1 to 3 substituents selected from Cl, Br, F, OMe, NO<sub>2</sub> and CF<sub>3</sub>.

49. (currently amended) A method of treating or preventing neoplasms in a patient comprising administering to the patient a compound of formula:



or a pharmaceutically acceptable salt or solvate thereof wherein:

Ar represents: pyridyl which may be unsubstituted or substituted with one or more substituents selected from the group consisting of: (a) Cl, (b) Br, (c) F, (d) OH, (e) NO<sub>2</sub>, (f) CF<sub>3</sub>, (g) C<sub>1-4</sub> alkyl, (h) SCH<sub>3</sub>, (i) NHCOCH<sub>3</sub>, (j) N(R<sup>6</sup>)(R<sup>8</sup>) wherein R<sup>6</sup> and R<sup>8</sup> are the same or different and each represents H or C<sub>1-4</sub> alkyl, (k) OR<sup>10</sup> wherein R<sup>10</sup> represents a saturated or unsaturated C<sub>1-6</sub> straight or branched hydrocarbyl group which may be unsubstituted or substituted with from 1 to 3 substituents selected from Cl, Br, F, OMe, NO<sub>2</sub> and CF<sub>3</sub>, and (l) -OCOR<sup>11</sup> wherein R<sup>11</sup> represents a saturated or unsaturated C<sub>1-6</sub> straight or branched hydrocarbyl group or a phenyl group;

R represents OH, OR<sup>10</sup> or OCOR<sup>11</sup> wherein R<sup>10</sup> and R<sup>11</sup> are as defined above; and R<sup>1</sup> represents H or a C<sub>1-6</sub> straight or branched hydrocarbyl group which may be unsubstituted or substituted with from 1 to 3 substituents selected from Cl, Br, F, OMe, NO<sub>2</sub> and CF<sub>3</sub>.

50. (original) The method of claim 49, wherein the neoplasms are located in the uterus, ovary, or breast.

51. (original) The method of claim 48, wherein the cancer is a paclitaxel or docetaxel resistant cancer.

52. (canceled)

53. (canceled)

54. (currently amended) A method of treating or preventing menopausal disorders and osteoporosis in a patient comprising administering to the patient a compound of formula:

55. (original) A pharmaceutical composition comprising a compound of claim 31 and a pharmaceutically acceptable excipient.

56. (canceled)

57. (canceled)